## DRUG DISCRIMINATION UNDER TWO CONCURRENT FIXED-INTERVAL FIXED-INTERVAL SCHEDULES

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Pigeons were trained to discriminate 5.0 mg/kg pentobarbital from saline under a two-key concurrent fixed-interval (FI) 100-s FI 200-s schedule of food presentation, and later under a concurrent FI 40-s FI 80-s schedule, in which the FI component with the shorter time requirement reinforced responding on one key after drug administration (pentobarbital-biased key) and on the other key after saline administration (saline-biased key). After responding stabilized under the concurrent FI 100-s FI 200-s schedule, pigeons earned an average of 66% (after pentobarbital) to 68% (after saline) of their reinforcers for responding under the FI 100-s component of the concurrent schedule. These birds made an average of 70% of their responses on both the pentobarbital-biased key after the training dose of pentobarbital and the saline-biased key after saline. After responding stabilized under the concurrent FI 40-s FI 80-s schedule, pigeons earned an average of 67% of their reinforcers for responding under the FI 40 component after both saline and the training dose of pentobarbital. These birds made an average of 75% of their responses on the pentobarbital-biased key after the training dose of pentobarbital, but only 55% of their responses on the saline-biased key after saline. In test sessions preceded by doses of pentobarbital, chlordiazepoxide, ethanol, phencyclidine, or methamphetamine, the dose-response curves were similar under these two concurrent schedules. Pentobarbital, chlordiazepoxide, and ethanol produced dose-dependent increases in responding on the pentobarbital-biased key as the doses increased. For some birds, at the highest doses of these drugs, the dose-response curve turned over. Increasing doses of phencyclidine produced increased responding on the pentobarbital-biased key in some, but not all, birds. After methamphetamine, responding was largely confined to the saline-biased key. These data show that pigeons can perform drug discriminations under concurrent schedules in which the reinforcement frequency under the schedule components differs only by a factor of two, and that when other drugs are substituted for the training drugs they produce dose-response curves similar to the curves produced by these drugs under other concurrent interval schedules.

Key words: drug discrimination, concurrent fixed-interval schedules, pentobarbital, chlordiazepoxide, ethanol, phencyclidine, methamphetamine, key peck, pigeons

In drug-discrimination experiments, the schedule of reinforcement is a major determinant of the shape of the dose–response curve when other doses of the training drug, or doses of other drugs, are substituted for the training drug. When responding is maintained by fixed-ratio (FR) schedules, dose–response curves usually are quantal in individual animals; that is, almost all responses occur on one key after each dose. However, when responding is maintained by interval schedules, dose–response curves are usually are graded; that is, responses are distributed on both keys after some drug doses.

These findings are consistent with data from simple FR and simple fixed-interval (FI) schedules (Massey, McMillan, & Wessinger, 1992), both FI and FR components of multi-

ple schedules (Snodgrass & McMillan, 1991;

As it is usually conducted, the drug-discrimination procedure is a conditional discrimination with both response choices available concurrently (if drug has been administered respond on Operandum A, if no drug has been administered respond on Operandum B). Snodgrass and McMillan (1991) suggest-

McMillan & Hardwick, 1996), concurrent FR FR schedules (McMillan & Li, 1999a), concurrent FI FI schedules (McMillan, Li, & Hardwick, 1997), and concurrent variable-interval (VI) VI schedules (Snodgrass & McMillan, 1996). Although most of these experiments were conducted using pigeons, some of these findings have been replicated with rats (McMillan & Hardwick, 2000). In most of the experiments, pentobarbital has served as the training drug, but these effects have been produced with other training drugs (Massey et al., 1992; McMillan, Cole-Fullenwider, Hardwick, & Wenger, 1982).

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ed that the schedule of reinforcement in drug-discrimination experiments might have characteristics of a concurrent schedule under some conditions. For example, at doses of the training drug different from those administered before training sessions, the presence or absence of the training drug may be difficult to discriminate. Under such conditions, the schedule may become analogous to a concurrent schedule because the drug stimulus does not signal reliably which response alternative will produce the reinforcer. This observation led to a series of experiments to study drug discrimination under concurrent reinforcement schedules. In these experiments, quantal dose-response curves in individual animals have been produced under concurrent FR FR schedules (McMillan & Li, 1999a), and graded dose-response curves have been produced under concurrent FI FI schedules (McMillan & Li, 1999b; McMillan et al., 1997) and under concurrent VI VI schedules (Snodgrass & McMillan, 1996), as predicted by the generalized matching law (Baum, 1979).

In experiments on drug discrimination under concurrent FI FI schedules, pigeons were trained to discriminate 5.0 mg/kg pentobarbital from saline under a concurrent FI 240s FI 60-s schedule of food presentation (Mc-Millan et al., 1997). Drug discrimination was established under this schedule, although there was some degree of undermatching (proportionally more responses occurred on the key on which responses were reinforced under the FI 240-s schedule than would be predicted by perfect matching of the proportion of responses made on that key to the proportion of reinforcers delivered for responding on that key) after saline training sessions. Analysis of cumulative response records showed that responding on the key programmed under the FI 60-s component of the concurrent schedule was characterized by a pause followed by a short acceleration of responding to a terminal rate to produce the reinforcer, whereas responding on the key programmed under the FI 240-s component of the schedule was characterized by short high-rate bursts of responding during the postreinforcement pauses on the other key. When other drugs were substituted for pentobarbital and the birds were tested under a concurrent FI 150-s FI 150-s schedule of food

presentation, graded dose-response curves were generated for pentobarbital, chlordiazepoxide, ethanol, and phencyclidine, with increasing doses of each of these drugs producing increased responding on the pentobarbital-biased key with two exceptions. First, for some birds the pentobarbital doseeffect curve turned over and began to descend after high doses of pentobarbital; second, the phencyclidine dose-response curve did not reach the same high level of responding on the pentobarbital-biased key as did the other drugs. In contrast, after methamphetamine the dose-response curve was flat, with most responses occurring on the saline-biased key.

Although McMillan et al. (1997) produced the predicted graded dose-response curves in drug-substitution experiments, it was possible that the obtained effects depended on the actual schedule values used in these experiments. In a follow-up study (McMillan & Li, 1999b), drug discrimination was established in two groups of pigeons under a concurrent FI 15-s FI 285-s schedule. One group of pigeons were the same birds used by Mc-Millan et al. (1997), and therefore they had a history of responding under the concurrent FI 60-s FI 240-s schedule, whereas the other group of birds was trained only under the concurrent FI 15-s FI 285-s schedule. The concurrent FI 15-s FI 285-s schedule was chosen because Davison and Jones (1995) suggested that the generalized matching law is a poor discriptor of extreme choice, which they defined as a concurrent schedule on which 90% or more of the reinforcers were produced by responding on one of the two response alternatives. Indeed, under conditions in which 80% of the reinforcers were produced by responses on one of the two response alternatives, matching behavior has been obtained under concurrent FI FI schedules (Shimp, 1971). In the experiments by McMillan and Li (1999b), when responding stablized under the concurrent FI 15-s FI 285s schedule, pigeons in both groups made 75% to 85% of their responses on the key on which responding was reinforced under the FI 15-s component of the schedule (undermatching); however, when the schedule was changed to a concurrent FI 150-s FI 150-s schedule for drug-substitution experiments, the presence or absence of pentobarbital con-

tinued to control the pattern of responding of the birds with the extensive training history, but the responding of the birds without this history came under control of the changed reinforcement schedule rapidly so that responding occurred almost equally often on the two response keys during these sessions. Under the concurrent FI 150-s FI 150-s schedule, the dose-response curves based on data from the entire session were flat. However, if data were used only from the first minute of the test sessions under concurrent FI 150 s FI 150 s before the schedule change assumed control of the behavior, dose-response curves for pentobarbital were graded for both the pigeons with previous experience under the concurrent FI 60-s FI 240s schedule and the birds without this history. Thus, even after training under extreme values of the concurrent FI 15-s FI 285-s schedule and under conditions in which schedule changes disrupted stimulus control by the training drug under a concurrent FI 150-s FI 150-s schedule, the concurrent FI FI schedules continued to generate the graded doseresponse curves predicted by the matching law.

In the current experiments, we extended the generality of our findings to concurrentschedule values in which the durations of the component FI schedules were less different from each other: concurrent FI 40 s FI 80 s and FI 100 s FI 200 s. Both of these schedules maintain the same 2:1 ratio of reinforcer availability under the two components of the concurrent schedule, but the absolute schedule values differed. These characteristics permitted determination of whether drug discrimination could be established when there was only a 2:1 ratio of reinforcer availability under the shorter interval component compared to the longer interval component. These schedule characteristics also allowed determination of whether absolute durations of the concurrent FI FI schedule values produced differences in response patterns when the ratio of reinforcers programmed for delivery under the component FI schedules was constant. In previous experiments, it has been shown that pigeons can discriminate differences in reinforcer ratios even smaller than 2:1 under concurrent FI FI schedules (White & Davison, 1973); however, these experiments did not involve drug discrimination.

Pentobarbital was selected as the training drug for these experiments so that the results could be compared directly to our previous experiments in which pentobarbital was established as the discriminative stimulus under concurrent schedules (McMillan & Hardwick, 2000; McMillan & Li, 1999b; McMillan et al., 1997; Snodgrass & McMillan, 1996). Chlordiazepoxide and ethanol were substituted for pentobarbital in generalization tests because these drugs have been reported to substitute as discriminative stimuli for pentobarbital in drug-discrimination studies (Colpaert, Desmedt, & Janssen, 1976). Methamphetamine was chosen because it has not substituted for pentobarbital as a discriminative stimulus, and phencyclidine was chosen because it has substituted partially for pentobarbital in drug-discrimination tests (McMillan & Hardwick, 1996).

#### **METHOD**

Subjects

Five adult male White Carneau pigeons (Palmetto Pigeon Plant) were used in these experiments. Birds P257, P259, and P260 had been used in previous experiments. Bird P347 was added to this group for all experiments. Birds P347 and P380 were experimentally naive. When Bird P259 died, Bird P380 was added for the concurrent FI 40-s FI 80-s schedule. The pigeons were individually housed with free access to food and water in a temperature- and humidity-controlled room that was maintained under a 12:12 hr light/ dark cycle. After 100% body weights were determined over a 2-week period, the pigeons were reduced to, and maintained at, approximately 80% of these weights for the duration of the study. Supplemental food was provided after experimental sessions as necessary to maintain the 80% body weights (range, 421 to 515 g).

## Apparatus

The experimental chamber was a Gerbrands Model G5610-A pigeon test cage enclosed in a Gerbrands Model G7211 soundand light-attenuating cubicle. Two 28-V DC lights illuminated the experimental chamber during the session except during a food cycle

when a light over the food hopper was illuminated. On the front panel of the cage, three Gerbrands response keys (Model G7311) were mounted 7 cm apart, 20 cm above the grid floor. The center key was not used in these experiments and was dark at all times. When operative, the left key was blue and the right key was yellow. The opening to a Gerbrands food hopper, which allowed access to mixed grain, was centered between the response keys at floor level. A Gateway microcomputer, located in a room adjacent to the room containing the experimental chamber, controlled the reinforcement schedule and recorded the data through a MED Associates interface.

### Procedure

The training of Birds P257, P259, and P260 has been described by McMillan et al. (1997). The 2 experimentally naive pigeons were trained using similar procedures. Briefly, the pigeons were trained to peck the blue left response key and the yellow right response key by an autoshaping procedure. After responding had been established on both keys, the FI schedules were introduced. In the present experiments, 5.0 mg/kg pentobarbital served as the training drug. Experiments were conducted under the concurrent FI 100-s FI 200s schedule first. Following an intramuscular injection of 5.0 mg/kg pentobarbital or saline, birds were placed in the test chamber and a 10-min presession period followed. During this 10 min, the chamber lights were extinguished and key pecks were not recorded. At the end of the presession period, the houselights and keylights were illuminated and the schedule contingencies were initiated. During these discrimination training sessions, both the left and right keys were transilluminated, and a different and independent FI schedule was operative on each key. Completion of either of the FI components resulted in delivery of the reinforcer (4-s access to mixed grain). After administration of the training drug, the FI 100-s component was programmed on one key and the FI 200-s component was programmed on the other. The key associated with each schedule component was counterbalanced across birds. After saline administration the schedules for the two keys were reversed. Training sessions lasted 40 min. Responding was maintained

under this concurrent FI FI schedule throughout the first study with the exception of control and test sessions, which will be described later.

To prevent immediate reinforcement of switching between keys (Catania, 1966), a changeover delay (COD) of 3 s was imposed, such that a response could not produce a reinforcer unless it occurred at least 3 s after the bird switched from responding on one key to responding on the other key. Training sessions were conducted 6 days per week. During these training sessions pentobarbital and saline administration alternated.

Test sessions were interspersed with training sessions when the performance was stable. During these test sessions, conducted on Tuesdays and Fridays, other doses of pentobarbital and other doses of other drugs were administered, instead of saline or the training dose of pentobarbital. Training sessions continued on the other 4 days. The procedure during test sessions was similar to that during training sessions, except that during test sessions a concurrent FI 150-s FI 150-s schedule of reinforcement was in effect in an attempt to prevent the training schedule from controlling the pattern of responding on the two keys. This FI value was chosen because it is intermediate between the FI 100-s and the FI 200-s schedule values used during the training sessions. In addition to the other doses of pentobarbital and other drugs that were administered during test sessions, saline and the pentobarbital training dose were administered during sessions under the concurrent FI 150-s FI 150-s schedule prior to and after the determination of each dose-response curve. These test sessions were intended to measure the effect of the schedule change on the stability of the stimulus control of behavior by saline and by the training dose of pentobarbital when the schedule was changed to that used during test sessions. Drug-substitution tests were conducted in single test sessions on different days, with single observations of each dose level conducted in each subject. All dose levels for a single drug were administered in a randomized order before exposure to a different drug. The order of drug testing was pentobarbital, phencyclidine, methamphetamine, ethanol, and chlordiazepoxide. The test sessions also lasted 40 min.

On completion of these manipulations, the schedule was changed to a concurrent FI 40 s FI 80 s for Birds P257, P260, and P347. P380 was trained to key peck as noted previously and then was placed on the concurrent FI 40-s FI 80-s schedule. Next, the drug manipulations described above with the concurrent FI 100-s FI 200-s schedules were repeated in the same order. During the drug-substitution tests in this part of the experiment, a concurrent FI 60-s FI 60-s schedule was in effect.

The number of CODs, the number of responses on each key, the time spent responding under each FI component and the number of reinforcers earned under each schedule component were recorded. Other measures were derived from these data. One such measure was the percentage of responses on the pentobarbital-biased key. The pentobarbital-biased key was defined as the key associated with the shorter FI component of the concurrent schedule (FI 100 s under the concurrent FI 100-s FI 200-s schedule and FI 40 s under the concurrent FI 40-s FI 80-s schedule) after the administration of pentobarbital during the training sessions. The saline-biased key was defined in the same manner as the key associated with the shorter FI component after administration of saline during the training sessions. The percentage of responses on the pentobarbital-biased key was derived by dividing the number of responses emitted on the pentobarbital-biased key by the sum of responses emitted on both keys and converting the proportion to a percentage. A second derived measure was the percentage of time allocated to responding on the pentobarbital-biased key. A response on the pentobarbital-biased key began recording the accumulation of time until a response on the saline-biased key switched the recording of the accumulation of time to the other kev. The total time accumulated after responses on the pentobarbital-biased key was divided by the accumulated time spent responding on both keys to calculate the percentage of time spent responding on the pentobarbitalbiased key. The total number of responses on a key was divided by the time spent responding on that key to calculate the rate of responding on the pentobarbital-biased key and the saline-biased key. The sum of the number of responses on the two keys was divided by the total time spent responding on

the two keys to calculate the overall rate of responding.

Pentobarbital sodium (Sigma) at doses of 1.0 to 13.0 mg/kg, phencyclidine hydrochloride (PCP, National Institute on Drug Abuse) at doses of 0.1 to 1.8 mg/kg, methamphetamine hydrochloride (Sigma) at doses of 0.3 to 3.0 mg/kg, chlordiazepoxide hydrochloride (Hoffman-La Roche) at doses of 0.3 to 10.0 mg/kg, and ethanol at doses of 0.3 to 3.0 g/kg were studied. All drugs except ethanol were dissolved in 0.9% physiological saline to a concentration allowing an injection volume of 1 ml/kg and were administered intramuscularly into a breast muscle. Physiological saline was used for vehicle control injections. Doses are expressed as the salt forms of the drugs, except for ethanol. All drugs were administered 10 min before the session. The pigeons were placed in the test chamber during the 10-min presession period. Ethanol (100% w/v) was diluted to a 10% w/v solution with tap water. The 10% ethanol solution or tap water, which was used as the vehicle control, was administered 15 min prior to session initiation through a rubber tube that passed down the esophagus into the proventriculus.

#### **RESULTS**

Table 1 shows, for each bird under the FI 100-s component of the concurrent FI 100-s FI 200-s schedule, the mean number of reinforcers delivered, the mean number of responses made, and the mean time allotted to responding during the last 20 sessions before test sessions were initiated. Birds earned 61% to 71% of their reinforcers for responding on the pentobarbital-biased key after pentobarbital and 67% to 69% of their reinforcers for responding on the saline-biased key after saline administration during these training sessions. Birds made 61% to 79% of their responses on the pentobarbital-biased key after pentobarbital and allocated 66% to 79% of their time to responding on that key. The birds made 54% to 86% of their responses on the saline-biased key after saline and spent 62% to 73% of their time responding on that key. Some birds slightly undermatched the ratio of responses to the ratio of reinforcers delivered following pentobarbital (P347) or saline (P257 and P260), whereas other birds

 $Table\ 1$  Individual-subject and group means of 10 pentobarbital training sessions and 10 saline training sessions under the concurrent FI 100-s FI 200-s schedule for responding, reinforcers delivered and time allocated to responding on the pentobarbital-biased key, and the number of CODs.

|      | Pentobarbital training sessions |           |       |      |           |       |       |           |       |      |  |  |  |
|------|---------------------------------|-----------|-------|------|-----------|-------|-------|-----------|-------|------|--|--|--|
|      | R                               | Responses |       | R    | Reinforce | ers   | Tin   | e (second | ls)   |      |  |  |  |
| Bird | Pent                            | Sal       | %Pent | Pent | Sal       | %Pent | Pent  | Sal       | %Pent | CODs |  |  |  |
| P347 | 1,328                           | 732       | 65    | 19   | 8         | 71    | 1,817 | 470       | 79    | 109  |  |  |  |
| P257 | 1,706                           | 447       | 79    | 22   | 10        | 68    | 1,543 | 694       | 69    | 52   |  |  |  |
| P259 | 1,071                           | 685       | 61    | 12   | 7         | 61    | 1,668 | 659       | 72    | 75   |  |  |  |
| P260 | 1,546                           | 508       | 75    | 21   | 12        | 64    | 1,502 | 766       | 66    | 70   |  |  |  |
| M    | 1,413                           | 593       | 70    | 19   | 9         | 66    | 1,633 | 647       | 72    | 77   |  |  |  |

overmatched the ratio of responses to the ratio of reinforcers delivered. Bird P259 perfectly matched the percentage of responses on the pentobarbital-biased key to the percentage of reinforcers delivered for responses on that key. On average, the ratio of responses on the key programmed to deliver responses under the shorter FI component and the ratio of time spent responding on that key were close to the ratio of reinforcers delivered for responding on each key (after pentobarbital, 66% of reinforcers, 70% of responses, and 72% of time allocation were associated with the pentobarbital-biased key; after saline, 68% of reinforcers, 70% of responses, and 68% of time allocation were associated with the saline-biased key). These values are close to perfect matching (Baum, 1979). The mean number of CODs was higher after saline administration than after pentobarbital administration, but this effect was not consistent across birds. During training sessions, Birds P259 and P260 responded at higher overall rates after saline than after pentobarbital, whereas the other 2 birds responded at similar rates after saline and pentobarbital (Table 1).

Figure 1 shows cumulative response records for Bird P347 for performance under the concurrent FI 100-s FI 200-s schedule. Performance during training sessions is shown in the left column. During training sessions with both saline and pentobarbital, responding under the FI 100-s component of the schedule was characterized by a postreinforcement pause, followed by a short period of accelerated responding to a terminal rate that was maintained until delivery of the reinforcer. Under the FI 200-s component, re-

sponding was characterized by long pauses followed by bursts of responding. These bursts usually occurred during the postreinforcement pause in responding on the other key, especially after saline administration. Although the response bursts on the key on which reinforcer delivery was programmed under the FI 200-s component usually occurred during the postreinforcement pause on the other key, responses under the FI 200s component also occurred at other times to cause occasional interruptions in reponding on the key programmed under the FI 100-s component of the schedule, especially for pentobarbital training sessions. Other pigeons produced similar patterns of responding.

Table 2 shows stable data under the concurrent FI 40-s FI 80-s schedule for each bird. Birds earned 66% to 68% of their reinforcers both for responding on the pentobarbital-biased key after pentobarbital administration and for responding on the saline-biased key after saline administration. Birds made 60% to 85% of their responses on the pentobarbital-biased key after pentobarbital and allocated 57% to 70% of their time to responding on that key. The pigeons made 43% to 75% of their responses on the saline-biased key after saline and allocated 41% to 57% of their time to responding on that key. After pentobarbital administration, small amounts of both undermatching and overmatching of the ratio of responses to reinforcers delivered were observed in individual birds; however, after saline administration undermatching occurred for Birds P380, P260 (for both responses and time allocation), and P257 (for time allocation). The number of CODs was

Table 1 (Extended)

|       |           |      | Sa   | aline train                | ing sessions | 3    |       |      |      |
|-------|-----------|------|------|----------------------------|--------------|------|-------|------|------|
|       | Responses |      | F    | Reinforcers Time (seconds) |              |      |       |      |      |
| Pent  | Sal       | %Sal | Pent | Sal                        | %Sal         | Pent | Sal   | %Sal | CODs |
| 265   | 1,774     | 86   | 11   | 22                         | 67           | 618  | 1,649 | 73   | 56   |
| 862   | 1,447     | 63   | 10   | 21                         | 68           | 629  | 1,637 | 72   | 113  |
| 481   | 1,765     | 78   | 10   | 21                         | 69           | 831  | 1,542 | 66   | 50   |
| 1,360 | 1,613     | 54   | 11   | 22                         | 67           | 850  | 1,412 | 62   | 161  |
| 742   | 1,650     | 70   | 11   | 22                         | 68           | 732  | 1.560 | 68   | 95   |

very similar after saline and the training dose of pentobarbital. During training sessions, all birds responded at higher overall rates after saline than after pentobarbital.

Figure 2 shows cumulative response rec-

ords for Bird P347 under the concurrent FI 40-s FI 80-s schedule. During training sessions after administration of both saline and pentobarbital, responding under the FI 40-s component of the concurrent FI 40-s FI 80-s

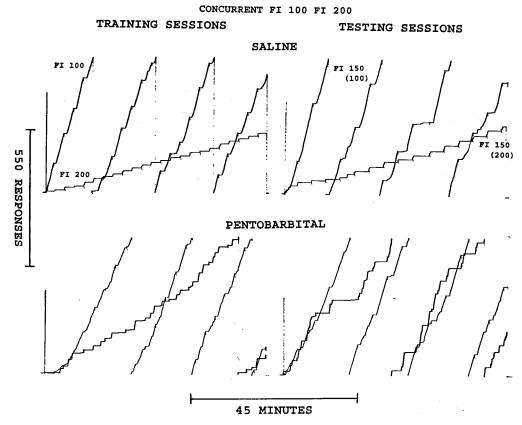


Fig. 1. Cumulative response records under the concurrent FI 100-s FI 200-s schedule for Bird P347 during training sessions (left column) and test sessions (second column) after saline (top row) or 5.0 mg/kg pentobarbital (bottom row) administration. Downward deflections of the response pen represent reinforcer delivery. The cumulative records have been overlaid to permit comparisons of patterns of responding on the two keys.

 $Table\ 2$  Individual-subject and group means of 10 pentobarbital training sessions and 10 saline training sessions under the concurrent FI 40-s FI 80-s schedule for responding, reinforcers delivered and time allocated to responding on the pentobarbital-biased key, and the number of CODs.

| Bird | Pentobarbital training sessions |     |       |             |     |       |       |            |       |      |  |  |  |
|------|---------------------------------|-----|-------|-------------|-----|-------|-------|------------|-------|------|--|--|--|
|      | Responses                       |     |       | Reinforcers |     |       | Tim   | ne (second | ls)   |      |  |  |  |
|      | Pent                            | Sal | %Pent | Pent        | Sal | %Pent | Pent  | Sal        | %Pent | CODs |  |  |  |
| P347 | 1,830                           | 327 | 85    | 42          | 20  | 68    | 1,129 | 478        | 70    | 75   |  |  |  |
| P257 | 900                             | 600 | 60    | 42          | 20  | 68    | 951   | 657        | 59    | 82   |  |  |  |
| P380 | 1,874                           | 608 | 75    | 41          | 21  | 66    | 932   | 674        | 58    | 123  |  |  |  |
| P260 | 1,027                           | 229 | 81    | 41          | 20  | 67    | 915   | 694        | 57    | 75   |  |  |  |
| M    | 1,408                           | 441 | 75    | 42          | 20  | 67    | 982   | 626        | 61    | 89   |  |  |  |

schedule was characterized by a postreinforcement pause, followed by a short period of accelerated responding to a terminal rate that was maintained until delivery of the reinforcer. Under the FI 80-s component, responding was characterized by longer pauses followed by bursts of responding. These bursts usually occurred during the postreinforcement pause in responding on the other key after both saline and pentobarbital administration. Similar patterns of responding were observed in other pigeons.

Figure 3 shows the dose–response curve for the effects of pentobarbital during test sessions. Points at C, which represent mean percentages of responding when the reinforcement schedule was changed from concurrent FI 100 s FI 200 s to FI 150 s FI 150 s, or concurrent FI 40 s FI 80 s to FI 60 s FI 60 s for these test sessions, show that these schedule changes did not disrupt control by the training dose of pentobarbital. This observation is confirmed by the cumulative response records shown in Figures 1 and 2, in which the patterns of responding are shown for Bird P347 when the schedule was changed from concurrent FI 100 s FI 200 s to concurrent FI 150 s FI 150 s (Figure 1) or from concurrent FI 40 s FI 80 s to concurrent FI 60 s FI 60 s (Figure 2). Patterns of responding under the FI 100-s component now changed to FI 150 s continued to show a typical FI pattern of responding (pause followed by acceleration to a high terminal rate of responding), except that the terminal rate of responding lasted longer due to the lengthening of the schedule component. Under the FI 200-s component, now also changed to FI 150 s, patterns of responding were similar to

those during training sessions (long pauses followed by bursts of responding that often occurred during the postreinforcement pause on the other key). The rates of responding for Bird P347 were considerably higher after pentobarbital under the schedule component on which responses were reinforced under the FI 150-s schedule used during testing after having been reinforced under the FI 200-s component during training sessions (Figure 1); however, this effect was not observed consistently for Bird P347 or for the other birds.

When the pentobarbital dose–response curve was determined, low doses of pentobarbital produced responding on the pentobarbital-biased key at percentages close to those seen during saline training sessions (Figure 3). Increasing doses of pentobarbital produced an increased percentage of responding on the pentobarbital-biased key under both schedules. At the higher doses of pentobarbital, there was a tendency for the dose–response curve to turn over and begin to descend for Bird P260 under both schedules and perhaps also for Bird P380 under the concurrent FI 60-s FI 60-s schedule after training under concurrent FI 40 s FI 80 s.

Figure 4 shows dose–response curves for pentobarbital for the percentage of time allocated to responding on the pentobarbital-biased key under each schedule. When the birds were trained under the concurrent FI 100-s FI 200-s schedule and tested under the concurrent FI 150-s FI 150-s schedule, the time-allocation data were similar to the data for percentage of responses on the pentobarbital-biased key. That is, the percentage of time spent responding on the pentobarbital-

Table 2 (Extended)

|      |           |      |      | Saline trai | ning session | s    |            |      |      |
|------|-----------|------|------|-------------|--------------|------|------------|------|------|
|      | Responses |      | ]    | Reinforcer  | rs           | Tiı  | me (second | s)   |      |
| Pent | Sal       | %Sal | Pent | Sal         | %Sal         | Pent | Sal        | %Sal | CODs |
| 298  | 867       | 75   | 21   | 41          | 66           | 698  | 910        | 57   | 71   |
| 400  | 586       | 59   | 20   | 40          | 67           | 890  | 730        | 45   | 81   |
| 931  | 744       | 45   | 19   | 41          | 68           | 908  | 709        | 44   | 160  |
| 452  | 344       | 43   | 19   | 41          | 67           | 951  | 664        | 41   | 80   |
| 520  | 635       | 55   | 20   | 41          | 67           | 861  | 753        | 47   | 98   |

biased key increased with dose, except for Bird P260, for which the curve turned over after the highest dose of pentobarbital. However, when the birds were trained under the concurrent FI 40-s FI 80-s schedule and tested under the concurrent FI 60-s FI 60-s sched-

ule, the percentage of time spent on the two schedule components became less different from each other than occurred with the percentage of responses. This similarity in percentage of time spent responding on each schedule component when the schedule was

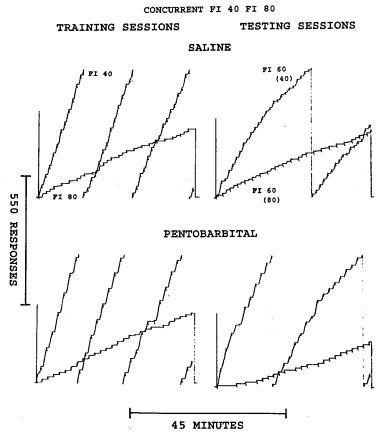


Fig. 2. Cumulative response records under the concurrent FI 40-s FI 80-s schedule for Bird P347. The details are as in Figure 1.

## **PENTOBARBITAL**

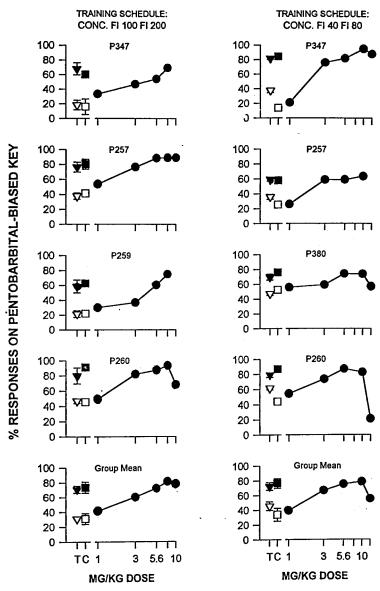


Fig. 3. Dose–response curves for the effects of pentobarbital on the percentage of responses on the pentobarbital-biased key on which, during training sessions, responses were reinforced under the FI 100-s component of the concurrent FI 100-s FI 200-s schedule (first column) and the FI 40-s component of the concurrent FI 40-s FI 80-s schedule (second column). Brackets at T (training sessions) show  $\pm 1$  standard deviation around the mean based on the data obtained during training sessions. Brackets at C (control sessions for schedule changes) show  $\pm 1$  standard deviation around the mean based on the control sessions in which the schedule was changed to concurrent FI 150 s FI 150 s (first column) or to concurrent FI 60 s FI 60 s (second column), which were the schedules used during determination of the dose–response curves. The filled circles show the pentobarbital dose–response curve with single observations made at each dose level. The filled triangles and squares above T and C show the effects of 5.0 mg/kg pentobarbital and saline during training and control sessions. The open triangles and squares above T and C show the effects of saline injections during training and control sessions.

### **PENTOBARBITAL**

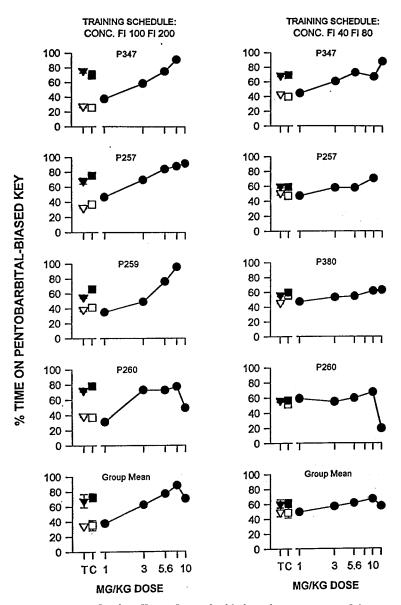


Fig. 4. The dose–response curve for the effects of pentobarbital on the percentage of time spent responding on the pentobarbital-biased key. Details as in Figure 3.

changed to concurrent FI 60 s FI 60 s and saline or the training dose of pentobarbital was administered caused the pentobarbital dose–response curve to be much flatter for time-allocation percentages than had occurred for the percentage of responses on the pentobarbital-biased key. Nevertheless, most birds showed a gradually increasing per-

centage of time spent responding on the pentobarbital-biased key as the dose of pentobarbital increased, except that again the dose-response curve descended for Bird P260 after the highest dose of pentobarbital. The raw data on which Figures 3 and 4 are based are shown in Appendixes A and B.

Figure 5 shows dose-response curves for

### **PHENCYCLIDINE**

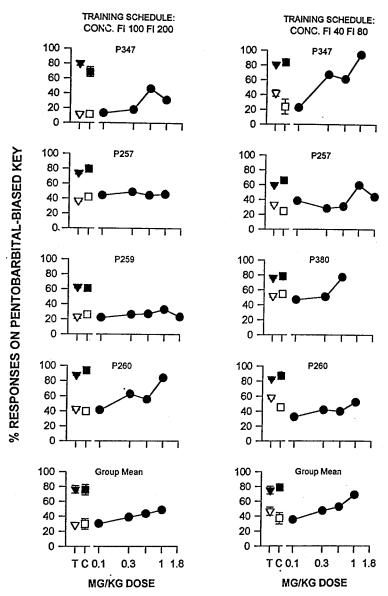


Fig. 5. The dose–response curve for the effects of phencyclidine on the percentage of responses on the pentobarbital-biased key. Details as in Figure 3.

the effects of phencyclidine on the percentage of responses on the pentobarbital-biased key under the two concurrent schedules. The effects of phencyclidine depended on the reinforcement schedule and the subject. In some instances, phencyclidine substituted fully for pentobarbital (P260 under concurrent FI 150 s FI 150 s; P347, P257, and P380 under

concurrent FI 60 s FI 60 s), in other instances there was partial substitution (P347 under concurrent FI 150 s FI 150 s), and in other instances there was no substitution (P257 and P259 under concurrent FI 150 s FI 150 s; P260 under concurrent FI 60 s FI 60 s). There was no consistent pattern as to which birds or schedules showed full, partial, or no

#### **METHAMPHETAMINE**

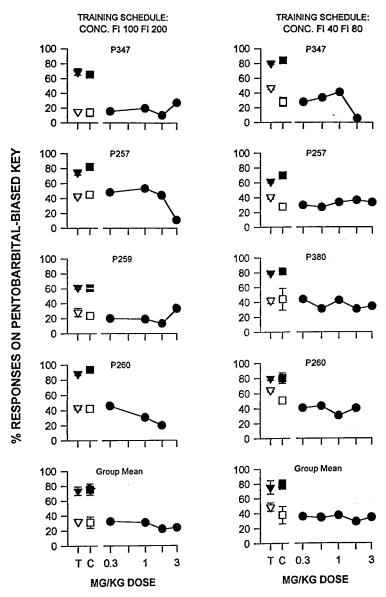


Fig. 6. The dose–response curve for the effects of methamphetamine on the percentage of responses on the pentobarbital-biased key. Details as in Figure 3.

substitution of phencyclidine for pentobarbital across reinforcement schedules.

Figure 6 shows the dose–response curves for the effects of methamphetamine on the percentage of responses on the pentobarbital-biased key under the two reinforcement schedules. Methamphetamine did not substitute for pentobarbital in any bird under either concurrent schedule. In a number of instances (P257 and P260 under concurrent FI 150 s FI 150 s and P347 and P260 under concurrent FI 60 s FI 60 s), responding on the pentobarbital-biased key fell below the level seen during saline training sessions after the administration of methamphetamine.

Figure 7 shows the dose–response curves

### **ETHANOL**

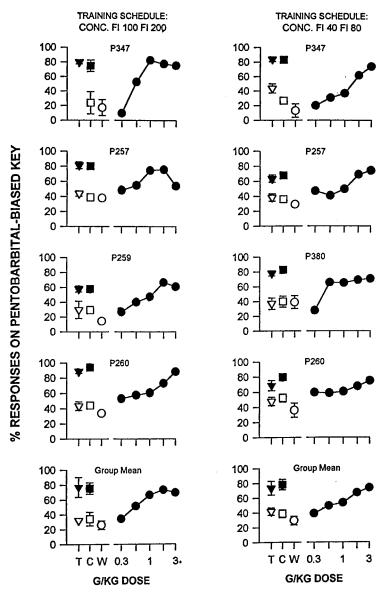


Fig. 7. The dose–response curve for the effects of ethanol on the percentage of responses on the pentobarbital-biased key. The abscissa is in grams per kilogram. Points above W show the effects of gavage with water. Other details as in Figure 3.

for substitution of ethanol for pentobarbital. Administration of water (points at W) produced responding on the saline-biased key. Increasing doses of ethanol increased responding on the pentobarbital-biased key, with full substitution occurring at doses of 1 to 3 g/kg. The dose–response curve turned

over in Bird P257 under the concurrent FI 150-s FI 150-s schedule.

Figure 8 shows the dose–response curves for the substitution of chlordiazepoxide for pentobarbital. Increasing doses of chlordiazepoxide increased responding on the pentobarbital-biased key under both concurrent

## **CHLORDIAZEPOXIDE**

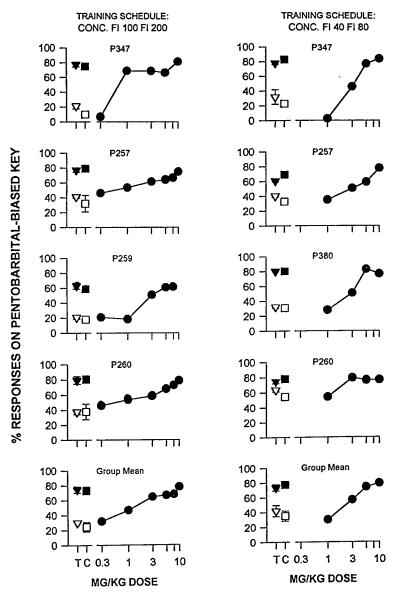


Fig. 8. The dose–response curve for the effects of chlordiazepoxide on the percentage of responses on the pentobarbital-biased key. Details as in Figure 3.

schedules. Full substitution of chlordiazepoxide for the training dose of pentobarbital occurred in all birds. The raw data on which Figures 5 through 8 are based are shown in Appendixes A and B.

Appendixes A and B also show the effects of these five drugs on the number of responses emitted, the time allocated to responding

under each schedule component, and the total number of CODs for each pigeon during the substitution tests. The total number of responses emitted was decreased by higher doses of all drugs under both concurrent reinforcement schedules, demonstrating that the full dose–effect curve had been explored for these drugs. Changeover delays, a measure of switching between keys, also usually decreased at high doses, although there were exceptions. The number of responses emitted and the number of CODs calculated across subjects for each drug were positively correlated (range, 0.44 to 0.81), except that the correlation between total responses and CODs was only 0.14 under the concurrent FI 100-s FI 200-s schedule after phencyclidine administration. These data suggest that at least some of the changes in CODs could be accounted for by decreases in overall rates of responding.

#### DISCUSSION

Although reinforcers were available only twice as frequently under the shorter FI component of each of these concurrent FI FI schedules, pigeons acquired the drug discrimination under both concurrent schedules. In the first experiment, pigeons learned to discriminate 5.0 mg/kg pentobarbital from saline under a concurrent FI 100-s FI 200-s schedule of food presentation. When responding stabilized, birds obtained about twice as many reinforcers under the FI 100-s component as under the FI 200-s component after both the training dose of pentobarbital and saline. Thus the actual ratio of reinforcers delivered was close to the programmed ratio under the concurrent FI 100-s FI 200-s schedule. Similar detection of small differences in reinforcement rate in the components of a concurrent VI VI schedule not involving drug discrimination have been reported previously (Charman & Davison, 1983).

In previous experiments using concurrent schedules of reinforcement, undermatching (a lower percentage of responses on the response alternative with the higher reinforcement rate than the percentage of reinforcers delivered for responses on that response alternative) is the rule (Davison & Nevin, 1999). Some degree of both undermatching and overmatching of responses and time-allocation ratios to reinforcer ratios occurred under the concurrent FI 100-s FI 200-s schedule in the present experiments, but the effects were usually small and were not consistent across birds or stimulus conditions. On average, the percentage of responses under the FI 100-s component of the concurrent schedule was close to the percentage of reinforcers delivered under that component. Thus, as a group the birds were close to matching responses to reinforcers delivered.

Under the concurrent FI 40-s FI 80-s schedule the pigeons also discriminated the presence or absence of 5.0 mg/kg of pentobarbital, with every bird earning almost exactly twice as many reinforcers under the FI 40-s component of the schedule as under the FI 80-s component. Thus, the ratio of reinforcers delivered under the two schedule components again was close to the ratio programmed by the reinforcement schedule. As in the concurrent FI 100-s FI 200-s schedule, some degree of both undermatching and overmatching occurred. In pentobarbital training sessions, some birds overmatched and some undermatched, but these effects were modest and depended on whether the measure of matching was responding or time allocation. In saline training sessions, 3 birds (Table 2) undermatched to a considerable extent on time allocation (P257) or on both time allocation and responding (P380 and P260).

The conditions under which undermatching occurs under concurrent reinforcement schedules in drug-discrimination experiments remain unclear. In our original experiments we used a concurrent FI 60-s FI 240-s schedule and found that pigeons usually matched response ratios and time-allocation ratios to reinforcer ratios after pentobarbital sessions, but that undermatching consistently occurred during saline training sessions (Mc-Millan et al., 1997). More recently, pigeons trained to discriminate pentobarbital from saline were studied under a concurrent FI 15-s FI 285-s reinforcement schedule. Undermatching of response ratios and time-allocation ratios to reinforcer ratios was consistently observed for both saline and pentobarbital training sessions (McMillan & Li, 1999b). In experiments on concurrent schedules that did not involve drug discrimination, White and Davison (1973) studied a wide range of concurrent FI FI schedule values. They concluded that matching occurred under these schedules when typical FI patterns of responding occurred under both schedule components or neither schedule component. This result is different from ours, in which matching occurred despite differences in response patterns under the FI components of the concurrent schedule. The data in Figures 1 and 2 for Bird P347 suggest that this pigeon did not exhibit consistent or pronounced undermatching, although the cumulative records show typical FI patterns of responding during the shorter FI components of the concurrent schedule and break-and-run responding during the longer FI components.

Under the present two concurrent schedules, the effects were similar when other doses and other drugs were substituted for the training dose of pentobarbital. Increasing doses of pentobarbital produced increased responding on the pentobarbital-biased key under both concurrent schedules. Occasionally, the pentobarbital dose-response curves descended after high doses. The inverted Ushaped dose-response curve occurred more frequently when the birds were studied under the concurrent FI 40-s FI 80-s schedule than under the FI 100-s FI 200-s schedule. As has been reported by others, phencyclidine produced a range of effects on responding under these schedules including no substitution, partial substitution, and full substitution for pentobarbital (McMillan, 1982; Snodgrass & McMillan, 1991). In contrast, methamphetamine did not substitute for pentobarbital, which is also consistent with other reports (McMillan & Li, 1999a; Witkin, Carter, & Dykstra, 1980). Other investigators have reported generalization from pentobarbital to chlordiazepoxide and ethanol (De Vry & Slangen, 1986; Grech & Balster, 1993; Jarbe & McMillan, 1983; Overton, 1966), which is also consistent with the findings of the present study. Thus, the substitution of other drugs for the training drug did not appear to be greatly influenced by the differences in concurrent-schedule values used in the present experiments.

In a number of instances, after the administration of methamphetamine the pigeons responded less often on the pentobarbital-biased key than they did after saline during training sessions. We have argued previously (Snodgrass & McMillan, 1996) that such responding may indicate a more salient stimulus of "not pentobarbital" than does saline, although other explanations such as an amphetamine-induced perseveration (Randrup & Munkvad, 1967) on one key are equally plausable. The opportunity to observe such

effects may be an advantage of the use of concurrent schedules to study drug discrimination, because the procedures do not produce the floor and ceiling effects seen with most drug-discrimination procedures.

The data from the present experiments suggest that previous difficulties in studying drug discrimination in rats using concurrent reinforcement schedules (McMillan & Hardwick, 2000) may reflect a difference between rats and pigeons. In rats, a concurrent VI 40s VI 80-s schedule maintained strong control over responding, but the training drug provided only weak control over responding when the drug-substitution tests were conducted under a concurrent VI 50-s VI 50-s schedule. When the training schedule was concurrent VI 60 s VI 240 s and drug-substitution tests were conducted under a concurrent VI 150-s VI 150-s schedule, stimulus control by the drug was improved. It was suggested that changes in shorter duration VI schedules might be more easily detected than changes in longer duration VI schedules. Therefore, schedule control might replace control by the drug stimulus more rapidly when short-duration VI schedules are manipulated than would occur with longer VI schedules. In the present experiments, there was no difference in stimulus control by the training drug under the two concurrent schedules despite a difference in the duration of the components of the two schedules. Unfortunately, the present experiments are far from conclusive on this point, because the present experiments used concurrent FI FI schedules with a ratio of 2:1 in the delivery of reinforcers under these FI components and the experiments with rats used concurrent VI VI schedules with a ratio of 4:1 in the delivery of reinforcers under the VI components. Thus, the differences between rats and pigeons may reflect differences between FI and VI schedules or differences between the ratios of reinforcer delivery under the reinforcement schedules that were studied.

As indicated previously, there is now a database suggesting that the maintenance of drug discrimination under interval schedules generates graded dose–response curves, whereas the maintenance of drug discrimination under ratio schedules generates quantal dose–response curves. The present experiments provide data both sup-

porting and not supporting this supposition. If the dose-response curves for pentobarbital, chlordiazepoxide, and ethanol (all drugs for which complete substitution occurred in most birds) are considered, the curves usually appear to be graded. Exceptions in which the curves are quantal occurred under concurrent FI 60 s FI 60 s after pentobarbital for P257 (Figure 3), after chlordiazepoxide for P260 (Figure 8), and perhaps after ethanol for P380 (Figure 7). Thus quantal dose-response curves occurred only two or three times out of a total of 24. However, in many instances in which the dose-response curve is graded, low doses produced responding on the saline-biased key after which a higher dose caused responding to shift to the pentobarbital-biased key without intermediate responding, despite the graded shape of the total doseresponse curve. The problem with studying shapes of dose-response curves under concurrent schedules in which the ratio of reinforcer delivery under the two schedule components is only 2:1 is the compression of the dose–response curve. It is difficult to determine if responding is graded or quantal when the training schedules have compressed the difference between responding on the drug-biased key and responding on the saline-biased key to such a narrow range. The fact that graded dose effects are seen so frequently even under these conditions is strong evidence that interval schedules do favor the occurrence of graded responding.

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# APPENDIX A

For each pigeon, under the concurrent FI 100-s FI 200-s schedule, the dose–response data for each drug are shown. The data are the number of changeover delays (CODs); the number of responses, reinforcers, and time (seconds) allocated to the pentobarbital (Pb) and saline (S) biased keys; and the percentage of responses and time emitted on the pentobarbital-biased key (%Pb).

|           |             |        | ]          | Responses |          | Reinf | orcers |       | Time  |      |
|-----------|-------------|--------|------------|-----------|----------|-------|--------|-------|-------|------|
| Pigeon    | Dose        | CODs   | Pb         | S         | % Pb     | Pb    | S      | Pb    | S     | % Pb |
| Pentobarb | oital (mg/k | g)     |            |           |          |       |        |       |       |      |
| P347      | 0.0         | 56     | 376        | 2,029     | 16       | 15    | 15     | 586   | 1,691 | 26   |
|           | 1.0         | 72     | 1,079      | 2,163     | 33       | 16    | 15     | 854   | 1,416 | 38   |
|           | 3.0         | 149    | 1,633      | 1,873     | 47       | 15    | 14     | 1,329 | 944   | 58   |
|           | 5.6         | 159    | 1,530      | 1,316     | 54       | 14    | 12     | 1,714 | 571   | 75   |
|           | 7.8         | 63     | 776        | 347       | 69       | 13    | 5      | 2,127 | 198   | 91   |
| P257      | 0.0         | 174    | 1,202      | 1,699     | 41       | 15    | 15     | 839   | 1,434 | 37   |
|           | 1.0         | 145    | 1,457      | 1,244     | 54       | 15    | 14     | 1,063 | 1,213 | 47   |
|           | 3.0         | 68     | 2,131      | 654       | 77       | 16    | 14     | 1,585 | 690   | 70   |
|           | 5.6         | 39     | 2,201      | 284       | 89       | 16    | 15     | 1,923 | 353   | 84   |
|           | 7.8         | 32     | 1,789      | 217       | 89       | 14    | 12     | 2,025 | 268   | 88   |
|           | 10.0        | 20     | 1,067      | 130       | 89       | 10    | 8      | 2,140 | 186   | 92   |
| P259      | 0.0         | 33     | 276        | 1,018     | 22       | 14    | 9      | 958   | 1,349 | 42   |
| F 259     | 1.0         | 98     | 1,244      | 2,890     | 30       | 14    | 15     | 801   | 1,476 | 35   |
|           | 3.0         | 63     | 881        | 1,500     | 30<br>37 | 13    | 11     | 1,130 | 1,170 | 49   |
|           | 5.6         | 63     | 948        | 621       | 60       | 8     | 7      | 1,788 | 549   | 77   |
|           | 7.8         | 13     | 948<br>215 | 72        | 75       | 8     | 7      |       | 92    | 96   |
|           |             |        |            |           |          |       |        | 2,291 |       |      |
| P260      | 0.0         | 209    | 1,615      | 1,898     | 45       | 13    | 15     | 845   | 1,433 | 37   |
|           | 1.0         | 157    | 1,446      | 1,480     | 49       | 13    | 15     | 714   | 1,565 | 31   |
|           | 3.0         | 60     | 2,040      | 450       | 82       | 15    | 16     | 1,659 | 612   | 73   |
|           | 5.6         | 34     | 1,395      | 205       | 87       | 15    | 16     | 1,650 | 622   | 73   |
|           | 7.8         | 34     | 2,269      | 155       | 94       | 15    | 14     | 1,765 | 515   | 77   |
|           | 10.0        | 65     | 1,415      | 654       | 68       | 10    | 13     | 1,135 | 1,169 | 49   |
| Chlordiaz | epoxide (n  | ng/kg) |            |           |          |       |        |       |       |      |
| P347      | 0.0         | 42     | 201        | 1,926     | 10       | 14    | 14     | 661   | 1,627 | 29   |
|           | 0.3         | 47     | 151        | 2,079     | 7        | 13    | 15     | 497   | 1,787 | 22   |
|           | 1.0         | 78     | 1,398      | 634       | 69       | 15    | 14     | 1,180 | 1,098 | 52   |
|           | 3.0         | 35     | 1,380      | 630       | 69       | 10    | 8      | 1,200 | 1,100 | 52   |
|           | 5.6         | 46     | 616        | 312       | 66       | 10    | 8      | 1,414 | 939   | 60   |
|           | 7.8         |        |            |           |          |       |        |       |       |      |
|           | 10.0        | 54     | 524        | 129       | 81       | 9     | 9      | 1,541 | 792   | 78   |
| P257      | 0.0         | 123    | 817        | 1,211     | 32       | 14    | 14     | 833   | 1,471 | 36   |
| 1 40.     | 0.3         | 130    | 1,583      | 1,843     | 46       | 15    | 14     | 880   | 1,398 | 39   |
|           | 1.0         | 105    | 1,809      | 1,561     | 54       | 14    | 15     | 1,124 | 1,174 | 49   |
|           | 3.0         | 130    | 1,312      | 816       | 62       | 15    | 14     | 1,142 | 1,134 | 50   |
|           | 5.6         | 78     | 1,372      | 762       | 64       | 12    | 13     | 1,228 | 1,068 | 53   |
|           | 7.8         | 57     | 2,257      | 1,129     | 67       | 13    | 12     | 1,390 | 871   | 61   |
|           | 10.0        | 110    | 2,790      | 938       | 75       | 16    | 15     | 1,526 | 743   | 67   |
| DOEO      | 0.0         | 44     | 353        | 1,685     | 18       |       | 15     | 654   |       | 29   |
| P259      |             |        |            |           |          | 15    |        |       | 1,624 |      |
|           | 0.3         | 30     | 246        | 942       | 21       | 15    | 10     | 747   | 1,550 | 33   |
|           | 1.0         | 59     | 610        | 2,719     | 18       | 16    | 15     | 525   | 1,746 | 23   |
|           | 3.0         | 53     | 1,675      | 1,620     | 51       | 15    | 16     | 1,317 | 998   | 57   |
|           | 5.6         | 58     | 810        | 524       | 61       | 11    | 12     | 1,347 | 923   | 59   |
|           | 7.8         | 63     | 860        | 534       | 62       | 9     | 11     | 1,670 | 634   | 72   |

# APPENDIX A

 $({\it Continued})$ 

|            |            |        | ]     | Responses |          | Reinf | orcers |       | Time         |          |
|------------|------------|--------|-------|-----------|----------|-------|--------|-------|--------------|----------|
| Pigeon     | Dose       | CODs   | Pb    | S         | % Pb     | Pb    | S      | Pb    | S            | % Pb     |
| P260       | 0.0        | 211    | 1,046 | 1,609     | 38       | 15    | 16     | 865   | 1,407        | 38       |
|            | 0.3        | 219    | 1,413 | 1,663     | 46       | 15    | 16     | 905   | 1,359        | 40       |
|            | 1.0        | 221    | 1,654 | 1,411     | 54       | 15    | 16     | 892   | 1,371        | 39       |
|            | 3.0        | 66     | 1,235 | 869       | 59       | 15    | 14     | 1,332 | 977          | 58       |
|            | 5.6        | 82     | 1,327 | 629       | 68       | 11    | 13     | 1,329 | 970          | 58       |
|            | 7.8        | 109    | 1,571 | 591       | 73       | 12    | 11     | 1,389 | 897          | 61       |
|            | 10.0       | 119    | 1,280 | 345       | 79       | 12    | 13     | 1,531 | 753          | 70       |
| Ethanol (g | g/kg)      |        |       |           |          |       |        |       |              |          |
| P347       | 0.00       | 47     | 564   | 1,927     | 24       | 14    | 13     | 734   | 1,551        | 32       |
|            | 0.30       | 33     | 99    | 935       | 10       | 10    | 8      | 474   | 1,851        | 20       |
|            | 0.56       | 80     | 1,580 | 1,420     | 53       | 13    | 11     | 1,656 | 645          | 72       |
|            | 1.00       | 38     | 2,391 | 511       | 82       | 15    | 14     | 1,767 | 513          | 78       |
|            | 1.80       | 31     | 530   | 153       | 78       | 10    | 9      | 2,205 | 165          | 93       |
|            | 3.00       | 30     | 444   | 146       | 75       | 9     | 8      | 2,103 | 259          | 89       |
| P257       | 0.00       | 161    | 1,107 | 1,717     | 39       | 15    | 15     | 865   | 1,434        | 38       |
| 1 20 .     | 0.30       | 132    | 1,430 | 1,519     | 48       | 15    | 15     | 850   | 1,421        | 37       |
|            | 0.56       | 144    | 1,682 | 1,377     | 55       | 14    | 14     | 944   | 1,336        | 41       |
|            | 1.00       | 113    | 2,100 | 711       | 75       | 13    | 12     | 1,322 | 970          | 58       |
|            | 1.80       | 129    | 2,340 | 748       | 75<br>76 | 15    | 14     | 1,559 | 716          | 69       |
|            | 3.00       | 43     | 567   | 670       | 46       | 8     | 9      | 1,876 | 477          | 80       |
| P259       | 0.00       | 37     | 553   | 1,271     | 29       | 15    | 15     | 678   | 1,606        | 30       |
| 1 233      | 0.30       | 45     | 643   | 1,759     | 27       | 13    | 15     | 789   | 1,486        | 35       |
|            |            | 45     | 569   | 853       | 40       | 13    | 13     | 1,086 |              |          |
|            | 0.56       | 24     | 265   | 293       |          | 7     | 8      | 1,699 | 1,199<br>638 | 48<br>73 |
|            | 1.00       |        |       |           | 47       |       |        | 1,099 |              |          |
|            | 1.80       | 68     | 1,605 | 802       | 67       | 15    | 12     |       | 1,045        | 54       |
|            | 3.00       | 62     | 1,023 | 651       | 61       | 11    | 12     | 1,166 | 1,138        | 51       |
| P260       | 0.00       | 241    | 1,108 | 1,388     | 44       | 16    | 15     | 815   | 1,453        | 36       |
|            | 0.30       | 243    | 2,236 | 1,970     | 53       | 14    | 15     | 1,023 | 1,241        | 45       |
|            | 0.56       | 280    | 2,224 | 1,636     | 58       | 15    | 14     | 1,092 | 1,176        | 48       |
|            | 1.00       | 263    | 2,267 | 1,471     | 61       | 15    | 16     | 1,062 | 1,190        | 47       |
|            | 1.80       | 118    | 2,187 | 811       | 73       | 16    | 15     | 1,394 | 874          | 61       |
|            | 3.00       | 66     | 3,114 | 417       | 88       | 14    | 15     | 1,621 | 658          | 71       |
| Methamph   | netamine ( | mg/kg) |       |           |          |       |        |       |              |          |
| P347       | 0.0        | 60     | 338   | 2,163     | 14       | 16    | 15     | 726   | 1,547        | 32       |
|            | 0.3        | 58     | 447   | 2,425     | 16       | 16    | 15     | 734   | 1,537        | 32       |
|            | 1.0        | 84     | 489   | 1,981     | 20       | 16    | 15     | 893   | 1,376        | 39       |
|            | 1.8        | 40     | 220   | 1,879     | 10       | 16    | 15     | 672   | 1,600        | 30       |
|            | 3.0        | 96     | 739   | 1,947     | 28       | 16    | 15     | 835   | 1,434        | 37       |
| P257       | 0.0        | 164    | 1,410 | 1,736     | 45       | 15    | 15     | 972   | 1,302        | 43       |
| 1 20 ,     | 0.3        | 153    | 1,317 | 1,406     | 48       | 15    | 15     | 1,163 | 1,108        | 51       |
|            | 1.0        | 170    | 1,259 | 1,103     | 53       | 15    | 14     | 1,190 | 1,084        | 52       |
|            | 1.8        | 105    | 515   | 649       | 44       | 12    | 14     | 814   | 1,476        | 36       |
|            | 3.0        | 61     | 270   | 2,154     | 11       | 8     | 10     | 417   | 1,908        | 18       |
| DOTO       | 0.0        | 51     | 502   |           | 24       | 14    | 16     | 657   |              |          |
| P259       |            |        |       | 1,705     |          |       |        |       | 1,623        | 29       |
|            | 0.3        | 62     | 548   | 2,200     | 20       | 14    | 16     | 681   | 1,593        | 30       |
|            | 1.0        | 93     | 668   | 2,841     | 19       | 15    | 16     | 485   | 1,785        | 21       |
|            | 1.8        | 32     | 194   | 1,261     | 13       | 10    | 13     | 251   | 2,053        | 11       |
|            | 3.0        | 67     | 850   | 1,736     | 33       | 13    | 14     | 809   | 1,479        | 35       |
| P260       | 0.0        | 183    | 1,102 | 1,503     | 42       | 15    | 16     | 738   | 1,531        | 33       |
|            | 0.3        | 156    | 1,274 | 1,511     | 32       | 15    | 16     | 664   | 1,603        | 29       |
|            | 1.0        | 40     | 75    | 170       | 31       | 12    | 2      | 192   | 2,148        | 8        |
|            | 1.8        | 9      | 25    | 100       | 20       | 11    | 1      | 49    | 2,301        | 2        |
| Phencyc    | lidine (mg | /kg)   |       |           |          |       |        |       |              |          |
| P347       | 0.0        | 51     | 266   | 2,061     | 12       | 15    | 15     | 697   | 1,578        | 31       |
|            | 0.1        | 38     | 329   | 2,181     | 13       | 16    | 15     | 653   | 1,619        | 29       |

## APPENDIX A

(Continued)

|        |      |      | ]     | Responses |      | Reinf | orcers |       | Time  |      |
|--------|------|------|-------|-----------|------|-------|--------|-------|-------|------|
| Pigeon | Dose | CODs | Pb    | S         | % Pb | Pb    | S      | Pb    | S     | % Pb |
|        | 0.3  | 42   | 505   | 2,612     | 18   | 14    | 14     | 706   | 1,576 | 31   |
|        | 0.56 | 52   | 1,292 | 1,558     | 46   | 15    | 13     | 1,195 | 1,090 | 52   |
|        | 1.0  | 80   | 657   | 1,472     | 31   | 13    | 12     | 1,138 | 1,159 | 50   |
| P257   | 0.0  | 115  | 1,264 | 1,779     | 42   | 14    | 15     | 809   | 1,468 | 36   |
|        | 0.1  | 126  | 1,446 | 1,826     | 44   | 15    | 15     | 881   | 1,395 | 39   |
|        | 0.3  | 93   | 1,789 | 1,849     | 49   | 15    | 14     | 814   | 1,460 | 36   |
|        | 0.56 | 61   | 1,239 | 1,542     | 44   | 13    | 13     | 927   | 1,363 | 41   |
|        | 1.0  | 62   | 1,257 | 1,495     | 46   | 14    | 14     | 1,113 | 1,171 | 49   |
| P259   | 0.0  | 44   | 404   | 1,287     | 26   | 12    | 15     | 856   | 1,442 | 37   |
|        | 0.1  | 36   | 436   | 1,544     | 22   | 14    | 14     | 981   | 1,303 | 43   |
|        | 0.3  | 42   | 543   | 1,509     | 26   | 13    | 15     | 838   | 1,451 | 37   |
|        | 0.56 | 42   | 841   | 2,240     | 27   | 12    | 14     | 823   | 1,470 | 36   |
|        | 1.0  | 52   | 983   | 2,057     | 33   | 11    | 14     | 682   | 1,611 | 30   |
| P260   | 0.0  | 157  | 1,117 | 1,523     | 40   | 15    | 16     | 793   | 1,478 | 35   |
|        | 0.1  | 49   | 1,319 | 1,692     | 41   | 15    | 15     | 751   | 1,518 | 33   |
|        | 0.3  | 109  | 2,735 | 1,647     | 63   | 15    | 15     | 1,285 | 994   | 56   |
|        | 0.56 | 90   | 1,905 | 1,443     | 56   | 14    | 13     | 1,114 | 1,162 | 49   |
|        | 1.0  | 30   | 934   | 184       | 84   | 14    | 9      | 2,127 | 206   | 91   |

# APPENDIX B

For each pigeon, under the concurrent FI 40-s FI 80-s schedule, the dose–response data for each drug are shown. The data are the number of changeover delays (CODs); the number of responses, reinforcers, and time (seconds) allocated to the pentobarbital (Pb) and saline (S) biased keys; and the percentage of responses and time emitted on the pentobarbital-biased key (%Pb).

|           |            |      | ]     | Responses |      | Reinf | orcers |       | Time  |      |  |
|-----------|------------|------|-------|-----------|------|-------|--------|-------|-------|------|--|
| Pigeon    | Dose       | CODs | Pb    | S         | % Pb | Pb    | S      | Pb    | S     | % Pb |  |
| Pentobarb | ital (mg/k | g)   |       |           |      |       |        |       |       |      |  |
| P347      | 0.0        | 55   | 207   | 1,288     | 14   | 24    | 32     | 748   | 1,121 | 39   |  |
|           | 1.0        | 68   | 470   | 1,749     | 21   | 27    | 24     | 937   | 1,176 | 44   |  |
|           | 3.0        | 56   | 1,440 | 450       | 76   | 28    | 23     | 963   | 626   | 61   |  |
|           | 5.6        | 56   | 1,561 | 346       | 82   | 26    | 24     | 1,160 | 434   | 73   |  |
|           | 10.0       | 24   | 1,305 | 67        | 95   | 17    | 2      | 1,156 | 568   | 67   |  |
|           | 13.0       | 35   | 1,621 | 222       | 88   | 23    | 24     | 1,457 | 191   | 88   |  |
| P257      | 0.0        | 66   | 301   | 880       | 25   | 26    | 27     | 862   | 980   | 47   |  |
|           | 1.0        | 54   | 325   | 925       | 26   | 27    | 27     | 743   | 835   | 47   |  |
|           | 3.0        | 70   | 940   | 666       | 59   | 26    | 25     | 919   | 671   | 58   |  |
|           | 5.6        | 62   | 857   | 601       | 59   | 28    | 26     | 911   | 666   | 58   |  |
|           | 10.0       | 41   | 529   | 301       | 64   | 25    | 18     | 1,147 | 478   | 71   |  |
| P380      | 0.0        | 131  | 824   | 740       | 52   | 27    | 28     | 879   | 707   | 56   |  |
| 1000      | 1.0        | 192  | 1,348 | 1,072     | 55   | 27    | 28     | 744   | 834   | 47   |  |
|           | 3.0        | 183  | 1,331 | 918       | 59   | 26    | 28     | 837   | 743   | 53   |  |
|           | 5.6        | 99   | 2,036 | 710       | 74   | 27    | 28     | 853   | 718   | 54   |  |
|           | 10.0       | 65   | 2,021 | 722       | 74   | 27    | 27     | 971   | 606   | 62   |  |
|           | 13.0       | 79   | 2,087 | 1,559     | 57   | 27    | 28     | 993   | 583   | 63   |  |
| P260      | 0.0        | 59   | 301   | 384       | 44   | 26    | 28     | 811   | 767   | 51   |  |
| 1,00      | 1.0        | 56   | 500   | 418       | 54   | 26    | 28     | 931   | 647   | 59   |  |
|           | 3.0        | 57   | 1,429 | 280       | 74   | 27    | 26     | 866   | 715   | 55   |  |
|           | 5.6        | 50   | 1,280 | 189       | 87   | 27    | 24     | 968   | 652   | 60   |  |
|           | 10.0       | 34   | 1,337 | 278       | 83   | 22    | 14     | 1,114 | 538   | 67   |  |
|           | 13.0       | 51   | 345   | 1,282     | 21   | 11    | 22     | 329   | 1,335 | 20   |  |

# APPENDIX B

 $({\it Continued})$ 

|            |                |          | ]            | Responses         |          | Reinf    | orcers   |                | Time       |          |
|------------|----------------|----------|--------------|-------------------|----------|----------|----------|----------------|------------|----------|
| Pigeon     | Dose           | CODs     | Pb           | S                 | % Pb     | Pb       | S        | Pb             | S          | % Pb     |
| Chlordiaze | epoxide (m     | ıg/kg)   |              |                   |          |          |          |                |            |          |
| P347       | 0.0            | 61       | 331          | 1,124             | 23       | 28       | 27       | 781            | 793        | 49       |
|            | 1.0            | 17       | 31           | 1,234             | 2        | 3        | 27       | 160            | 1,515      | 10       |
|            | 3.0            | 73       | 1,032        | 1,225             | 46       | 25       | 25       | 790            | 803        | 50       |
|            | 5.6            | 58       | 993          | 294               | 77       | 19       | 18       | 1,274          | 377        | 77       |
|            | 10.0           | 1        | 16           | 3                 | 84       | 2        | 0        | 1,789          | 3          | 100      |
| P257       | 0.0            | 62       | 415          | 855               | 33       | 26       | 27       | 756            | 830        | 48       |
|            | 1.0            | 55       | 469          | 867               | 35       | 26       | 27       | 694            | 889        | 44       |
|            | 3.0            | 59       | 639          | 622               | 51       | 23       | 24       | 645            | 960        | 40       |
|            | 5.6            | 66       | 569          | 391               | 59       | 22       | 22       | 943            | 674        | 58       |
|            | 10.0           | 75       | 1,501        | 421               | 78       | 23       | 25       | 993            | 570        | 64       |
| P380       | 0.0            | 57       | 305          | 691               | 30       | 26       | 28       | 670            | 908        | 42       |
|            | 1.0            | 57       | 297          | 768               | 28       | 27       | 28       | 624            | 950        | 40       |
|            | 3.0            | 62       | 640          | 618               | 51       | 27       | 28       | 777            | 797        | 49       |
|            | 5.6            | 66       | 1,583        | 326               | 83       | 27       | 28       | 979            | 593        | 62       |
|            | 10.0           | 69       | 1,428        | 426               | 77       | 26       | 26       | 899            | 686        | 57       |
| P260       | 0.0            | 54       | 545          | 454               | 54       | 27       | 28       | 848            | 727        | 54       |
|            | 1.0            | 55       | 706          | 590               | 54       | 25       | 27       | 866            | 719        | 55       |
|            | 3.0            | 53       | 1,225        | 318               | 79       | 27       | 27       | 832            | 745        | 53       |
|            | 5.6            | 56       | 1,051        | 324               | 76       | 27       | 27       | 890            | 688        | 56       |
|            | 10.0           | 59       | 1,187        | 357               | 77       | 27       | 26       | 941            | 642        | 59       |
| Ethanol (g | (/kg)          |          |              |                   |          |          |          |                |            |          |
| P347       | 0.00           | 52       | 171          | 1,038             | 13       | 20       | 27       | 562            | 1,051      | 35       |
|            | 0.30           | 52       | 217          | 846               | 20       | 26       | 27       | 772            | 810        | 49       |
|            | 0.56           | 83       | 630          | 1,419             | 31       | 28       | 27       | 831            | 749        | 53       |
|            | 1.00           | 63       | 537          | 918               | 37       | 25       | 26       | 812            | 778        | 51       |
|            | 1.80           | 88       | 1,294        | 797               | 62       | 22       | 26       | 940            | 673        | 58       |
|            | 3.00           | 14       | 230          | 80                | 74       | 14       | 7        | 1,319          | 410        | 76       |
| P257       | 0.00           | 70       | 382          | 932               | 29       | 28       | 27       | 700            | 885        | 43       |
|            | 0.30           | 61       | 688          | 767               | 47       | 27       | 27       | 767            | 811        | 49       |
|            | 0.56           | 89       | 687          | 979               | 41       | 26       | 27       | 771            | 824        | 48       |
|            | 1.00           | 60       | 612          | 620               | 50       | 23       | 21       | 806            | 816        | 50       |
|            | 1.80<br>3.00   | 55<br>22 | 1,003<br>514 | $\frac{450}{177}$ | 69<br>74 | 21<br>14 | 20<br>8  | 1,093<br>1,407 | 680<br>305 | 62<br>82 |
| D000       |                |          |              |                   |          |          |          |                |            |          |
| P380       | $0.00 \\ 0.30$ | 76<br>53 | 462<br>294   | 673<br>762        | 39<br>28 | 27<br>26 | 28<br>28 | 775<br>617     | 799<br>961 | 44<br>39 |
|            | 0.56           | 38       | 961          | 500               | 66       | 20<br>27 | 26<br>16 | 1,091          | 532        | 67       |
|            | 1.00           | 68       | 483          | 257               | 65       | 27       | 28       | 880            | 696        | 56       |
|            | 1.80           | 55       | 970          | 431               | 69       | 28       | 20       | 806            | 795        | 50       |
|            | 3.00           | 72       | 1,088        | 448               | 71       | 26       | 18       | 824            | 796        | 51       |
| P260       | 0.00           | 93       | 437          | 847               | 36       | 26       | 28       | 730            | 856        | 46       |
| 1200       | 0.30           | 70       | 723          | 489               | 60       | 26       | 27       | 977            | 603        | 61       |
|            | 0.56           | 112      | 1,095        | 771               | 59       | 26       | 27       | 773            | 805        | 49       |
|            | 1.00           | 102      | 886          | 572               | 61       | 26       | 25       | 903            | 685        | 57       |
|            | 1.80           | 116      | 1,269        | 606               | 68       | 26       | 27       | 844            | 741        | 53       |
|            | 3.00           | 64       | 852          | 284               | 75       | 27       | 27       | 920            | 657        | 58       |
| Methamph   | etamine (      | mø/kø)   |              |                   |          |          |          |                |            |          |
| P347       | 0.0            | 60       | 354          | 495               | 28       | 28       | 27       | 761            | 814        | 48       |
| 1011       | 0.3            | 62       | 409          | 1,070             | 28       | 27       | 27       | 809            | 765        | 51       |
|            | 0.56           | 75       | 475          | 941               | 34       | 28       | 27       | 868            | 705        | 55       |
|            | 1.0            | 83       | 710          | 1,018             | 41       | 26       | 26       | 723            | 878        | 45       |
|            | 1.8            | 28       | 78           | 1,323             | 6        | 6        | 26       | 115            | 1,549      | 7        |
| P257       | 0.0            | 60       | 341          | 886               | 28       | 26       | 27       | 736            | 850        | 46       |
|            | 0.3            | 56       | 313          | 743               | 30       | 27       | 27       | 803            | 775        | 51       |
|            | 0.56           | 57       | 331          | 902               | 27       | 25       | 27       | 665            | 921        | 42       |

# APPENDIX B

(Continued)

|            |            |      | ]     | Responses |      | Reinf | orcers |       | Time  |      |
|------------|------------|------|-------|-----------|------|-------|--------|-------|-------|------|
| Pigeon     | Dose       | CODs | Pb    | S         | % Pb | Pb    | S      | Pb    | S     | % Pb |
|            | 1.0        | 58   | 417   | 820       | 34   | 28    | 27     | 738   | 847   | 46   |
|            | 1.8        | 91   | 536   | 937       | 36   | 25    | 27     | 561   | 1,023 | 35   |
|            | 3.0        | 85   | 324   | 638       | 34   | 19    | 20     | 751   | 887   | 46   |
| P380       | 0.0        | 89   | 658   | 730       | 44   | 26    | 28     | 825   | 757   | 52   |
|            | 0.3        | 57   | 385   | 492       | 44   | 27    | 28     | 865   | 707   | 55   |
|            | 0.56       | 60   | 298   | 656       | 31   | 27    | 28     | 818   | 759   | 52   |
|            | 1.0        | 75   | 609   | 829       | 42   | 26    | 28     | 531   | 1,046 | 34   |
|            | 1.8        | 56   | 275   | 618       | 31   | 26    | 28     | 614   | 964   | 39   |
|            | 3.0        | 50   | 233   | 446       | 34   | 25    | 28     | 657   | 926   | 42   |
| P260       | 0.0        | 55   | 411   | 395       | 51   | 27    | 28     | 869   | 706   | 55   |
|            | 0.3        | 58   | 386   | 558       | 41   | 27    | 28     | 737   | 837   | 47   |
|            | 0.56       | 75   | 586   | 768       | 43   | 26    | 28     | 704   | 880   | 44   |
|            | 1.0        | 15   | 101   | 230       | 31   | 17    | 8      | 1,255 | 442   | 74   |
|            | 1.8        | 58   | 315   | 467       | 40   | 18    | 15     | 1,004 | 658   | 60   |
| Phencyclic | line (mg/k | cg)  |       |           |      |       |        |       |       |      |
| P347       | 0.0        | 51   | 296   | 1,006     | 24   | 25    | 27     | 476   | 1,031 | 31   |
|            | 0.1        | 54   | 367   | 1,238     | 23   | 27    | 27     | 639   | 936   | 41   |
|            | 0.3        | 54   | 1,711 | 821       | 68   | 27    | 23     | 999   | 596   | 63   |
|            | 0.56       | 68   | 1,389 | 868       | 62   | 27    | 26     | 901   | 684   | 57   |
|            | 1.0        | 32   | 1,183 | 65        | 95   | 27    | 5      | 1,569 | 102   | 94   |
| P257       | 0.0        | 59   | 283   | 870       | 24   | 27    | 27     | 501   | 855   | 35   |
|            | 0.1        | 72   | 520   | 834       | 38   | 27    | 25     | 756   | 824   | 48   |
|            | 0.3        | 66   | 434   | 1,097     | 28   | 28    | 27     | 603   | 790   | 43   |
|            | 0.56       | 52   | 389   | 869       | 31   | 27    | 27     | 712   | 866   | 45   |
|            | 1.0        | 56   | 722   | 487       | 60   | 24    | 25     | 860   | 740   | 54   |
|            | 1.8        | 49   | 512   | 643       | 44   | 23    | 24     | 808   | 797   | 50   |
| P380       | 0.0        | 86   | 834   | 685       | 54   | 27    | 28     | 794   | 653   | 54   |
|            | 0.1        | 57   | 475   | 540       | 47   | 27    | 28     | 816   | 758   | 52   |
|            | 0.3        | 59   | 490   | 475       | 51   | 27    | 27     | 810   | 725   | 53   |
|            | 0.56       | 104  | 2,125 | 620       | 77   | 26    | 26     | 1,058 | 531   | 67   |
| P260       | 0.0        | 54   | 324   | 391       | 45   | 27    | 28     | 555   | 577   | 47   |
|            | 0.1        | 54   | 196   | 410       | 32   | 26    | 28     | 780   | 797   | 49   |
|            | 0.3        | 63   | 462   | 639       | 42   | 25    | 28     | 766   | 819   | 48   |
|            | 0.56       | 145  | 853   | 1,275     | 40   | 24    | 25     | 708   | 908   | 44   |
|            | 1.0        | 93   | 1,588 | 1,459     | 52   | 26    | 24     | 852   | 743   | 53   |